

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (original): A microparticle comprising
a core,
at least one linking carrier on said core, wherein said linking carrier comprises a
biocompatible polymer, and
at least one radioactive therapeutic agent covalently bonded to said linking carrier;
wherein said microparticle has a diameter in the range of from 5 to 200 microns and said
microparticle is non-biodegradable.
2. (original): The particle of claim 1, wherein said microparticle is not water
swellable.
3. (original): The particle of claim 1, wherein said radioactive therapeutic agent is a
radionuclide or a radiopharmaceutical.
4. (original): The particle of claim 1, wherein said at least one radioactive
therapeutic agent is at least one radionuclide selected from the group consisting of an alpha-
emitting radionuclide, a beta-emitting radionuclide and a gamma-emitting radionuclide.

5. (original): The particle of claim 1, wherein said at least one radioactive therapeutic agent is an alpha-emitting radionuclide and a beta-emitting radionuclide.

6. (original): The particle of claim 1, wherein said at least one radioactive therapeutic agent is an alpha-emitting radionuclide, a beta-emitting radionuclide and a gamma-emitting radionuclide.

7. (original): The particle of claim 5, wherein said radioactive therapeutic agent is at least one radionuclide selected from the group consisting of iridium, radium, cesium, phosphorus, yttrium, rhenium, actinium, bismuth, astatine, technetium, indium, iodine, and carbon, nitrogen, fluorine, sodium, magnesium, aluminum, silicon, potassium, vanadium, manganese, gallium, niobium, iodine, lead, Y-90, Bi-213, At-211, I-123, I-125, I-131, At-211, Cu-67, Sc-47, Ga-67, Rh-105, Pr-142, Nd-147, Pm-151, Sm-153, Ho-166, Gd-159, Tb-161, Eu-152, Er-171, Re-186, Re-188, Tc-99m, In-111, Ga-67, Rh-105, I-123, Nd-147, Pm-151, Sm-153, Gd-159, Tb-161, Er-171, Re-186, Re-188, and Tl-201.

8. (original): The particle of claim 1, wherein said radioactive therapeutic agent is yttrium-90.

9. (original): The particle of claim 1, wherein said at least one radioactive therapeutic agent comprises a therapeutic radionuclide and an imaging or diagnostic radionuclide both chemically bonded to said linking carrier.

10. (original): The particle of claim 9, wherein said therapeutic radionuclide is a beta-emitting radionuclide and said an imaging or diagnostic radionuclide is a gamma-emitting radionuclide.

11. (original): The particle of claim 10, wherein said therapeutic radionuclide is yttrium-90 and said an imaging or diagnostic radionuclide is selected from the group consisting of indium-111 and Tc-99m.

12. (original): The particle of claim 1, wherein said radioactive therapeutic agent is bonded to said linking carrier through one or more spacer groups.

13. (original): The particle of claim 1, wherein said radioactive therapeutic agent is bound to said linking carrier by a chelator group.

14. (original): The particle of claim 13, wherein said chelator group is at least one selected from the group consisting of cyclohexyldiethylenetriaminepentaacetic acid ligand (CHX-DTPA), diethylenetriaminepentaacetic acid (DTPA), ethylenediaminetetraacetic acid (EDTA), 1,4,7,10-tetraazacyclododecane-N,N', N,"N"" tetraacetate (DOTA), tetraazacyclotetradecane-N,N", N"N"-tetraacetic acid (TETA), cyclohexyl 1,2-diamine tetraacetic acid (CDTA), ethyleneglycol-O,O'-bis(-2-aminoethyl)-N,N,N',N'-tetra-acetic acid (EGTA), N,N-bis(hydroxybenzyl)-e-thylenediamine-N,N'-diacetic acid (HBED), triethylenetetramine hexa-acetic acid (TTHA), hydroxyethyl diamine triacetic acid (HEDTA), hydroxyethylidene diphosphonate (HEDP), dimercaptosuccinic acid (DMSA), diethylenetriaminetetramethylenephosphonic acid (DTTP) and 1-(p-aminobenzyl)-DTPA, 1,6-

diamino hexane-N,N,N',N'-tetraacetic acid, DPDP, and ethylenebis (oxyethylenenitrilo)-tetraacetic acid.

15. (original): The particle of claim 13, wherein said radioactive therapeutic agent is yttrium-90 and said chelator group is DOTA.

16. (original): The particle of claim 1, wherein said core is non-ceramic and nonradioactively labeled.

17. (original): The particle of claim 1, wherein said core comprises a polymer selected from the group consisting of polyacrylate, ethylene-vinyl acetate polymer, an acyl substituted cellulose acetate, polyurethane, polystyrene, polyvinylchloride, polyvinyl flouride, poly(vinyl imidazole), chlorosulphonate polyolefin, polyethylene oxide, blends thereof, and copolymers thereof, a polyphosphazine, a poly(vinyl alcohol), a polyamide, a polycarbonate, a polyalkylene, a polyacrylamide, a polyalkylene glycol, a polyalkylene oxide, a polyalkylene terephthalate, a polyvinyl ether, a polyvinyl ester, a polyvinyl halide, polyvinylpyrrolidone, a polyglycolide, a polysiloxane, and copolymers thereof, an alkyl cellulose, an hydroxyalkyl cellulose, a cellulose ether, a cellulose ester, and a nitrocellulose.

18. (original): The particle of claim 1, wherein said at least one linking carrier is selected from the group consisting of a linear polymer, a branched polymer, and a dendromer polymer.

19. (original): The particle of claim 18, wherein said at least one linking carrier is a dendrimer.
20. (original): The particle of claim 19, wherein said dendrimer has a disulfide bond in its core.
21. (original): The particle of claim 19, wherein said dendrimer has a final external layer which is capped with a reactive group.
22. (original): The particle of claim 21, wherein said reactive group is an amine or carboxyl group.
23. (original): The particle of claim 21, wherein said reactive group is derivatized with at least one selected from the group consisting of a targeting entity and a therapeutic entity.
24. (original): The particle of claim 19, wherein said dendrimer has a terminal functional group which is accessible to a chelate containing compound which is capable of interacting with the functional groups.
25. (original): The particle of claim 24, wherein said functional group is at least one selected from the group consisting of ester group, ether group, thiol group, carbonyl group, hydroxyl group, amide group, carboxylic group, and imide group.

26. (original): The particle of claim 19, comprising multiple dendrimers, wherein said dendrimers are monodispersed.

27. (original): The particle of claim 18, wherein said linking carriers are linear polymers.

28. (original): The particle of claim 1, wherein said radioactive therapeutic agent is covalently bonded to said linking carrier via a bifunctional linker, carbodiimide condensation, or a disulfide bond formation.

29. (original): The particle of claim 1, wherein said particle does not leach radionuclide.

30. (original): The particle of claim 1, wherein said particle is spheroidal.

31. (original): The particle of claim 1, wherein said particle has a density in the range of from 1 to 4 gm/cm³.

32. (original): The particle of claim 1, wherein said particle has a density in the range of from 1 to 2 gm/cm³.

33. (original): The particle of claim 1, wherein said particle further comprises a second therapeutic agent or a diagnostic agent.

34. (original): The particle of claim 33, wherein said second therapeutic agent or said diagnostic agent is at least one selected from the group consisting of a metal chelate complex, a drug, a prodrug, a radionuclide, a boron addend, a labeling compound, a toxin, a cytokine, a lymphokine, a chemokine, an immunomodulator, a radiosensitizer, an asparaginase, a radioactive halogens, a chemotherapy drug and a contrast agent.

35. (currently amended): A particulate material comprising a plurality of the microparticle of claim 1 ~~microparticles having:~~

~~a core,~~

~~at least one linking carrier on said core, wherein said linking carrier comprises a biocompatible polymer, and~~

~~at least one radioactive therapeutic agent covalently bonded to said linking carrier;~~

~~wherein said microparticles have a diameter in the range of from 5 to 200 microns and said microparticles are non-biodegradable.~~

36. (original): The particulate material of claim 35, wherein said microparticles have a diameter in the range of from 8-100 microns.

37. (original): The particulate material of claim 35, wherein said microparticles have a diameter in the range of from 25-50 microns.

38. (original): The particulate material of claim 35, wherein said microparticles have a diameter in the range of from 20-30 microns.

39. (original): The particulate material of claim 35, wherein said microparticles have substantially equivalent particle sizes.

40. (original): The particulate material of claim 35, wherein said microparticles are sufficiently large so as to avoid phagocytosis.

41. (withdrawn and currently amended): A method of radiation therapy of a patient, which comprises administering to the patient at least one of the microparticles of claim 1, or the particulate material of claim 35, ~~wherein said microparticles comprise~~

~~a core,~~

~~at least one linking carrier on said core, wherein said linking carrier comprises a biocompatible polymer, and~~

~~at least one radioactive therapeutic agent covalently bonded to said linking carrier;~~

~~wherein said microparticle has a diameter in the range of from 5 to 200 microns and said microparticle is non-biodegradable.~~

42. (withdrawn): The method of radiation therapy of a patient of claim 41, wherein said microparticles are administered internally.

43. (withdrawn): The method of radiation therapy of a patient of claim 41, wherein the administration is direct to a lesion or through a vascular route.

44. (withdrawn): The method of radiation therapy of a patient of claim 41, wherein said radiation therapy treats cancer or a tumor.

45. (withdrawn): The method of radiation therapy of a patient of claim 44, wherein said cancer is primary or secondary cancer of the liver.

46. (withdrawn): The method of radiation therapy of a patient of claim 41, wherein said radiation therapy treats a highly vascularized tumor or a tumor which has a single dominant arterial vascular supply.

47. (withdrawn): The method of radiation therapy of a patient of claim 46, wherein said microparticles are injected into an artery supplying a tumor.

48. (withdrawn): The method of radiation therapy of a patient of claim 41, wherein said radiation therapy treats hepatic cancer, rheumatoid arthritis, a solid cancer, liver cancer, brain cancer, breast cancer and/or ovary cancer.

49. (withdrawn): The method of radiation therapy of a patient of claim 41, wherein said radiation therapy treats renal cell carcinoma, hepatoma, sarcomas, cancer of the head or neck, and/or a central nervous system tumor.

50. (withdrawn): The method of radiation therapy of a patient of claim 41, wherein said at least one radioactive therapeutic agent is at least one radionuclide selected from the group consisting of an alpha-emitting radionuclide, a beta-emitting radionuclide and a gamma-emitting radionuclide.

51. (withdrawn): The method of radiation therapy of a patient of claim 50, wherein said at least one radioactive therapeutic agent is an alpha-emitting radionuclide and a beta-emitting radionuclide.

52. (withdrawn): The method of radiation therapy of a patient of claim 51, wherein said at least one radioactive therapeutic agent is an alpha-emitting radionuclide, a beta-emitting radionuclide and a gamma-emitting radionuclide.

53. (withdrawn): The method of radiation therapy of a patient of claim 41, comprising radiation treatment and imaging or diagnosing.

54. (withdrawn): The method of radiation therapy of a patient of claim 53, wherein said imaging or diagnosing is during the life of the radiation.

55. (withdrawn): The method of radiation therapy of a patient of claim 53, wherein said imaging or diagnosing is post life of the radiation.

56. (withdrawn): The method of radiation therapy of a patient of claim 51, further comprising assaying the gamma radiation to determine the location of the microparticles in the patient.

57. (withdrawn): The method of radiation therapy of a patient of claim 41, wherein said particles are immobilized at a site of administration.

58. (withdrawn): The method of radiation therapy of a patient of claim 41, wherein said particles do not release a significant amount of radiation emitting radioisotope into the circulation system upon administration.

59. (withdrawn): The method of radiation therapy of a patient of claim 41, wherein said particles have a diameter of from 15 to 35 microns.

60. (withdrawn): A kit for preparing a microparticle treatment dose for a patient in need thereof, wherein said treatment dose comprises the particulate material of claim 35, wherein said kit comprises

particle cores, which do not comprise radionuclide,
linkers for attaching at least one radionuclide to said particle cores, and
instructions or a means for obtaining instructions for preparing said microparticle treatment dose.

61. (withdrawn): The kit for preparing a microparticle treatment dose of claim 60, wherein said kit contains a radionuclide.

62. (withdrawn): The kit for preparing a microparticle treatment dose of claim 60, wherein a radionuclide is provided separately from said kit.

63. (withdrawn): The kit for preparing a microparticle treatment dose of claim 60, further comprising at least one component selected from the group consisting of an inert pharmaceutically acceptable carrier, a formulating agent, an adjuvant, an active agent, water,

saline, a transfer ligand, a reducing agent, a lyophilization aid, a stabilization aid, a solubilization aid, a bacteriostat, a buffer, an X-ray contrast agent, an ultrasound contrast agent, and a metallopharmaceutical.

64. (withdrawn): The kit for preparing a microparticle treatment dose of claim 60, further comprising at least one component selected from the group consisting of a syringe, shielding, and imaging equipment.

65. (withdrawn): The kit for preparing a microparticle treatment dose of claim 60, wherein said kit comprises multiple types of cores and multiple types of linkers.

66. (withdrawn): A method of using the kit of claim 60 to prepare a microparticle treatment dose for a patient in need thereof,
determining the type and dosimetry of microparticle treatment needed from a prescription for said patient and preparing said microparticle treatment dose from said instructions or said means for obtaining instructions.

67. (withdrawn): A method of using the kit of claim 60 to prepare a microparticle treatment dose for a patient in need thereof,
determining the type and dosimetry of microparticle treatment needed from a prescription for said patient,
selecting a type of core from the cores included in said kit,
selecting a type of linker from the linkers included in said kit,
selecting a radionuclide and

preparing said microparticle treatment dose from said instructions or said means for obtaining instructions.

68. (withdrawn): The method of claim 60, wherein said microparticle treatment dose is made said kit at a location of administration or at a site proximate to the location of administration.

69. (withdrawn): The method of claim 60, wherein said location or said site is a local radiopharmacy, laboratory, hospital or physician's office.

70. (withdrawn): The method of claim 60, wherein said microparticle treatment dose are made said kit at a location of administration or at a site proximate to the location of administration.

71. (withdrawn): The method of claim 60, wherein said location or said site is a local radiopharmacy, laboratory, hospital or physician's office.

72. (withdrawn and currently amended): AThe microparticle of claim 1, wherein said microparticle contains comprising
a core, and
at least two radioactive therapeutic agents attached to said ~~core~~linking carrier.

73. (withdrawn and currently amended): The microparticle of claim 72, wherein said at least two radioactive therapeutic agents are independently selected from the group consisting of a therapeutic radionuclide and an imaging or diagnostic radionuclide.

74. (withdrawn and currently amended): The microparticle of claim 72, wherein at least one of said at least two radioactive therapeutic agents is a beta-emitting radionuclide and at least one of said at least two radioactive therapeutic agents is a gamma-emitting radionuclide.

75. (withdrawn and currently amended): The microparticle of claim 74, wherein said beta-emitting radionuclide is a therapeutic radionuclide and said gamma-emitting radionuclide is an imaging or diagnostic radionuclide.

76. (withdrawn and currently amended): The microparticle of claim 75, wherein said therapeutic radionuclide is yttrium-90 and said an imaging or diagnostic radionuclide is selected from the group consisting of indium-111 and Tc-99m.

77. (withdrawn and currently amended): The microparticle of claim 72, wherein said core is non-ceramic and nonradioactively labeled.

78. (withdrawn and currently amended): The microparticle of claim 72, wherein said core comprises a polymer selected from the group consisting of polyacrylate, ethylene-vinyl acetate polymer, an acyl substituted cellulose acetate, polyurethane, polystyrene, polyvinylchloride, polyvinyl flouride, poly(vinyl imidazole), chlorosulphonate polyolefin, polyethylene oxide, blends thereof, and copolymers thereof, a polyphosphazine, a poly(vinyl

alcohol), a polyamide, a polycarbonate, a polyalkylene, a polyacrylamide, a polyalkylene glycol, a polyalkylene oxide, a polyalkylene terephthalate, a polyvinyl ether, a polyvinyl ester, a polyvinyl halide, polyvinylpyrrolidone, a polyglycolide, a polysiloxane, and copolymers thereof, an alkyl cellulose, an hydroxyalkyl cellulose, a cellulose ether, a cellulose ester, and a nitrocellulose.

79. (withdrawn and currently amended): The microparticle of claim 72, wherein said at least two radioactive therapeutic agents are each attached to said core through a covalent bond.

80. (withdrawn and currently amended): The microparticle of claim 72, wherein said particle does not leach radionuclide.

81. (withdrawn and currently amended): The microparticle of claim 72, wherein said at least two radioactive therapeutic agents are independently selected from the group consisting of an alpha-emitting radionuclide, a beta-emitting radionuclide and a gamma-emitting radionuclide.

82. (withdrawn): A method of radiation therapy of a patient, which comprises administering to the patient microparticles, wherein said microparticles comprise the microparticle as claimed in claim 72.

83. (withdrawn): The method of radiation therapy of a patient of claim 82, comprising radiation treatment and imaging or diagnosing.

84. (withdrawn): The method of radiation therapy of a patient of claim 82, further comprising assaying the gamma radiation to determine the location of the microparticles in the patient.

85. (withdrawn): The particle of claim 1, wherein said microparticle has a diameter in the range of from 8 to 100.

86. (withdrawn): The particle of claim 1, wherein said microparticle has a diameter in the range of from 20 to 30.